

**REMARKS**

Claims 1-20 and 59-62 were pending in the application as of the issuance of the Office Action dated July 9, 2008. According to the foregoing amendments, claims 1, 7, 14-18 and 20 have been amended and claims 59-62 have been cancelled without prejudice to their prosecution in this or a subsequently filed application. Accordingly, after the amendments presented herein have been entered, claims 1-20 will remain pending in this application.

Support for the amendments to the claims may be found throughout the specification and in the claims as originally filed. Specifically, support for the amendment to claim 1 can be found at, for example, page 24, line 34 to page 25, line 7 and in claims 14-17, as originally filed.

No new matter has been added by the claim amendments. The amendments to the claims and the cancellation of certain claims should not be construed as an acquiescence to the validity of the Examiner's rejections and were done solely in the interest of expediting prosecution and allowance of the claims. Applicants reserve the right to pursue the claims as originally filed in one or more further applications.

**PRIORITY**

With respect to Applicants' priority claim, the Examiner states

[i]t is noted that applicants are claiming foreign priority to EP03/11411, however, no certified English translation was provided. In order to perfect benefit to this foreign document, applicants are urged to file a certified English translation.

Applicants respectfully point out that the present application claims priority to International Application No. PCT/US03/11411 and to U.S. Provisional Application No. 60/372762, not to EP03/11411. Applicants further submit that each of these priority applications was filed in and is available in English. In particular, Applicants submit that PCT/US03/11411 was published in English as International Publication No. WO03/088748. Accordingly, Applicants respectfully assert that the priority claim is accurate and, as such, Applicants respectfully request acknowledgment and confirmation of such priority claim.

**OBJECTIONS TO THE SPECIFICATION**

The Examiner objects to the specification on the grounds that "[t]he title of the invention is not descriptive." Applicants have amended the title in accordance with the Examiner's recommendation, thereby rendering the foregoing objection moot.

**OBJECTIONS TO THE CLAIMS**

The Examiner objects to claim 1 on the grounds that “the acronym HO-1 is not spelled out.” Applicants have amended claim 1 in accordance with the Examiner’s recommendation, thereby rendering the foregoing objection moot.

**INFORMATION DISCLOSURE STATEMENT**

Applicants gratefully acknowledge the Examiner’s indication that an Information Disclosure Statement has not yet been filed. Applicants submit that an Information Disclosure Statement will be filed shortly. Upon filing, Applicants respectfully request that the Examiner consider the references cited thereon and acknowledge such consideration by initialing the PTO Form SB/08 filed concurrently therewith.

**REJECTION OF CLAIMS 1-20 AND 59-62 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

The Examiner has rejected claims 1-20 and 59-62 under 35 U.S.C. § 112, second paragraph, as allegedly “failing to set forth the subject matter which applicant(s) regards as their invention.” Specifically, the Examiner is of the opinion that “[c]laims 1-20 and 59-62 are indefinite for the recitation of a ‘pharmaceutical composition’ absent a pharmaceutically acceptable carrier.”

Applicants respectfully disagree. Notwithstanding the foregoing, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner’s rejection, Applicants have amended the pending claims in accordance with the Examiner’s recommendation, *i.e.*, to include reference to “a pharmaceutically acceptable carrier,” thereby rendering the foregoing rejection moot.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection of pending claims 1-20 under 35 U.S.C. § 112, second paragraph.

**REJECTION OF CLAIMS 1-5, 8-15, 19-20 AND 59-62 UNDER 35 U.S.C. § 102(A)**

The Examiner has rejected claims 1-5, 8-15, 19-20 and 59-62 under 35 U.S.C. § 102(a) as being anticipated by Otterbein *et al.* (U.S. Patent No. 7,364,757) (hereinafter referred to as “Otterbein”). In particular, the Examiner is of the opinion that

Otterbein et al. teach that CO has potent anti-inflammatory effects and possibly suppresses intimal hyperplasia by inhibiting inflammation... In addition, Otterbein et al. teach that... 'Heme oxygenase-1 (HO-1) catalyzes the first step in the degradation of heme. HO-1 cleaves the .alpha.-meso carbon bridge of b-type heme molecules by oxidation to yield equimolar quantities of biliverdin Ixa, carbon monoxide (CO), and free iron. Subsequently, biliverdin is converted to bilirubin via biliverdin reductase, and the free iron is sequestered into ferritin (the production of which is induced by the free iron)'. The condition of intimal [*sic*] hyperplasia (thickening of Tunica intima of a blood vessel) is described in the reference as caused by transplantation or angioplasty...

Otterbein et al. also teach at paragraph 119, that 'alternatively or in addition, any of the products of metabolism by HO-1, e.g., bilirubin, biliverdin, iron and/or ferritin can be administered to a patient in conjunction with, or instead of, carbon monoxide in order to prevent or treat intimal hyperplasia. Further, the present invention contemplates that iron-binding molecules other than ferritin e.g., desferoxamine (DFO), iron dextran, and/or apo-ferritin, can be administered to the patient. Further still, the present invention contemplates that enzymes (e.g., biliverdin reductase) that catalyze the breakdown of any of these products can be inhibited to create/enhance the desired effect.'

At paragraph 127, Otterbein et al. links the condition to atherosclerosis and describes the surgical procedure of balloon angioplasty (vascular surgery).

Applicants respectfully disagree. Applicants respectfully submit that the claims as previously pending were novel over the teachings of Otterbein. Notwithstanding the foregoing, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended the pending claims to be directed to particular inflammatory disorders. Applicants submit that the subject matter of the pending claims is novel over the teachings of Otterbein. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection under 35 U.S.C. § 102(a).

**REJECTION OF CLAIMS 1-5, 8-15, 19-20 AND 59-62 UNDER 35 U.S.C. § 102(E)**

The Examiner has further rejected claims 1-5, 8-15, 19-20 and 59-62 under 35 U.S.C. §102(e) as being anticipated by Bach *et al.* (U.S. Patent No. 7,238,469) (hereinafter referred to as "Bach"). In particular, the Examiner is of the opinion that

Bach et al. teach Islet cell transplantation and complications with this process (i.e. non-specific inflammation). In addition, Bach et al. disclose that 'unfettered EC activation, as during acute and chronic inflammation can lead to EC injury and apoptosis. Bach et al. disclose that EC apoptosis is a prominent feature associated with acute and/or chronic inflammation such as it occurs during

hyperoxia, endotoxic shock, atherosclerosis, ischemia reperfusion injury, and acute or chronic graft rejection...

Further, Bach et al. teach iron-binding molecules other than ferritin e.g., desferoxamine (DFO), iron dextran, and/or apoferritin, can be administered to the patient. Any of the above compounds can be administered to the patient topically and/or systemically. Bach et al. also teach that the administration of nitric oxide (NO) to a patient, organ(s), tissue(s) and/or isolated cells in conjunction with administration of carbon monoxide, HO-1 and/or HO-1 associated compounds. This technique includes providing NO to the donor, the recipient, or the organ, tissue or cell ex vivo, in conjunction with the administration of HO-1 and/or all of the products of heme degradation, e.g., CO, biliverdin, bilirubin, iron, and ferritin (see paragraph 118).

Applicants respectfully disagree. Applicants respectfully submit that the claims as previously pending were novel over the teachings of Bach. Notwithstanding the foregoing, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended the pending claims to be directed to particular inflammatory disorders. Applicants submit that the subject matter of the pending claims is novel over the teachings of Bach. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection under 35 U.S.C. § 102(e).

**CONCLUSION**

In view of the foregoing remarks, reconsideration of the rejections and allowance of all pending claims is respectfully requested. If there are any remaining issues or if the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

The Commissioner is hereby authorized to charge any deficiency in the fees paid herewith, or credit any overpayment, to Deposit Account No. 12-0080, under Order No. CNZ-006US, from which the undersigned is authorized to withdraw.

Dated: **December 26, 2008**

Respectfully submitted,

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